Stem cell therapy for cerebral palsy

Stem cells – levels of risk

- The most common sources of stem cells studied in neurological applications are found in embryos, fetal tissue, birth tissues, cord blood and bone marrow. Some of these are tissue specific and require little processing; others are pluripotent and require laboratory manipulation and differentiation towards a dedicated lineage.
- In the future, adipose-derived stem cells and induced pluripotent stem cell-derived cells may emerge as therapeutic possibilities.
- The risk involved with injecting stem cells to treat neurological disorders is not well understood and requires further study.
- Points to consider:
  - Pluripotent stem cells such as embryonic or induced pluripotent stem cells (ESC or iPSC) form tumours. Dedicated lineages that are derived from these cells are less likely to form tumours than the pluripotent cells they are derived from.
  - Allogeneic cells (sourced from a donor) may provoke an immune response. Autologous cells (from the recipient’s own body) are immunologically safer.
  - Some stem cells are collected with no risk to the donor, some are collected invasively during medical procedures of varying risk levels.
  - Cell processing and preservation may involve toxic or allergenic chemicals.
  - Delivery of cells may involve inherent risks in addition to stem-cell related risks. The more invasive the delivery; for example by lumbar puncture or intracranially, the higher the risk. Intravenous delivery also involves many standard transfusion risks.
- Potential benefits may outweigh the risks involved, but the clinical evidence supporting any benefits is currently weak.

Use in Cerebral Palsy

- There is little evidence to prove that injected stem cells remain in the body long-term; the mechanism of action seems to be through chemical signalling with a range of growth factors and cytokines. Preclinical studies reveal that stem cells are immune-modulatory, protect neural cells from secondary cell death after injury, promote host stem cell proliferation and migration, and promote angiogenesis [1-3].
- With this information, but little clinical evidence, we suspect that stem cells may be more powerful and more suitable when applied to acute rather than chronic brain injury (cerebral palsy prevention) and for periods of developmental brain plasticity (early intervention).
- Far more research is needed to determine the appropriate type of stem cell, the optimum dose, the number of doses, whether cells should be combined with other treatments and many other unknowns. However, these questions must follow after the fundamental question – does stem cell therapy improve function for individuals with cerebral palsy?

Internationally

- There are currently eight ongoing international trials of stem cells derived from either bone marrow or cord blood for children with cerebral palsy, and two ongoing trials for adults with cerebral palsy.
Three small trials of fetal-derived cells injected into the brain to treat cerebral palsy have been published, including two open-label randomised controlled trials, demonstrating the procedure may be safe and possibly efficacious.

Six small studies of bone marrow stem cells injected intrathecally for cerebral palsy indicate relative safety of the procedure and possible efficacy. A total of 501 participants have been included in published studies to date.

Four safety studies of intravenous umbilical cord blood cells for cerebral palsy demonstrate that the procedure may be safe and possibly efficacious. A total of 348 participants have been included in all published studies to date.

A single published randomised controlled trial infusing unrelated donor cord blood cells into veins combined with other treatments showed:
- the treatment was safe in this combination,
- it may improve function for children with cerebral palsy,
- that younger children may benefit most.

Prevention of cerebral palsy
- One safety study of intravenous autologous umbilical cord blood cells for hypoxic-ischaemic encephalopathy demonstrated feasibility, safety and possible efficacy. Two similar trials are currently underway.

What is happening in Australia?
- An Australian collaboration has formed to trial intravenous infusion of a child’s own cord blood cells, or their matched sibling’s cord blood cells.
- The cord blood cell infusion would be combined with intensive rehabilitation therapy.
- The aims of this study will be to look at:
  - whether a cord blood cell injection is safe;
  - whether a large Australian trial of this use of stem cells is feasible and appropriate
- This study will gather information to guide future research; it will not give any definite answers as to the value of injecting stem cells into children with cerebral palsy.
- Ethics review is currently underway. We hope the small pilot trial will begin in late 2015.

Information about this and any other Australian trials will be circulated Australia-wide in Cerebral Palsy Register newsletters, through community organisations, private cord blood banks and the AusACPDM

More information
- Stem cell research
  - www.closerlookatstemcells.org
- National Stem Cell Foundation of Australia
  - www.stemcellfoundation.net.au
- Current clinical trials
  - www.clinicaltrials.gov
- Cerebral palsy registers
  - http://cpregister.com/
- Cord blood banks in Australia
  - www.abmdr.org.au
  - cordblood.cryosite.com
  - www.cellcare.com.au
  - www.stemlife.com

If you have any questions, please contact
Dr. Kylie Crompton
Research Officer MCRI
03 9936 6756 | kylie.crompton@mcri.edu.au
Useful reviews in the medical literature


Useful articles on ethics in this field


